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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/802,249

03/17/2004

Ralf Mauritz

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EXAMINER

LIU, SUE XU

ART UNIT

PAPER NUMBER

1639

MAIL DATE

DELIVERY MODE

05/22/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

10/802,249

Applicant(s)

MAURITZ ET AL.

Examiner

Sue Liu

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1639

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 March 2007.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) 4-11 and 23-26 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 12-22 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date 3/17/04;9/22/04.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

DETAILED ACTION

Please note the change of examiner for this application. (Please see the Conclusion paragraph for information on any future correspondence.)

Claim Status

Claims 1-26 are currently pending.

Claims 4-11, and 23-26 have been withdrawn.

Claims 1-3, and 12-22 are being examined in this application.

Election/Restrictions

1. Applicant's election without traverse of Group I (Claims 1-22) in the reply filed on 10/18/06 is acknowledged.
2. Claims 23-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 10/18/06.
3. Applicant's election without traverse of the following species:
 - A.) nucleic acids for the biopolymers;
 - B.) fluorescent groups, specifically, stilbene, as the detectable protecting groups;
 - C.) Compound (f) in Figure 5 as the core structure;

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in the reply filed on 10/18/06 and 3/6/07 is acknowledged. Accordingly, Claims 4-11 are withdrawn due to non-elected species.

Priority

4. This application claims foreign priority to EPO 03006098.2 (3/19/03).
5. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Information Disclosure Statement

6. The IDS filed on 3/17/04 and 9/22/04 have been considered. See the attached PTO 1449 forms.

Oath/Declaration

7. The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

Non-initialed and/or non-dated alterations have been made to the oath or declaration. See 37 CFR 1.52(c).

See page 3 of the Oath/Declaration filed on 7/21/04.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 15, 19 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15 recites the limitation "the building blocks" in line 1. There is insufficient antecedent basis for this limitation in the claim. The instant Claim 1 recites both "monomeric" and "oligomeric" (i.e. polymeric) "building blocks". However, the "general structural formulae (I) or (II)" depicted in claim 15 only seem to refer to "monomeric" building blocks. Thus, it is not clear to which "building blocks" (monomeric or polymeric recited in Claim 1) the term is referring.

Claim 19 recites the limitation "R3" in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 19 as written is dependent on the instant claim 12, which does not recite a R3 group.

Claim 22 recite the phrase "analogs thereof, and analogs containing additional amino groups". It is not clear of which entities the term "analogs" are referring. For example, the first occurring "analogs" in the claim can be construed to be analogs of "deaza", or analogs of each of the listed nucleoside base.

Claim Rejections - 35 USC § 102

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(Note: the instant claim numbers are in bold font.)

McGall et al

11. Claims 1-3, 12 and 13 are rejected under **35 U.S.C. 102(b)** as being anticipated by McGall et al (US 6,238,862; 05/29/2001).

The instant claims recite a “quality control method for manufacturing a biopolymer array comprising (a) synthesizing a plurality of different biopolymer species on an array from monomeric or oligomeric building blocks comprising detectable protecting groups, (b) cleaving off the detectable protecting groups, and (c) carrying out a determination of the detectable protecting groups on the array after cleavage in order to determine the efficacy of deprotection.”

McGall et al, throughout the patent, teach methods of quality control for manufacturing nucleic acid probe arrays (e.g. Abstract and Claim 1 of the reference), which reads on the quality control method of **clm 1**.

The reference teaches synthesizing nucleic acids using protected monomers (e.g. Claims 5, 12 and 23; col. 2, lines 40+; Figure 9), which reads on step (a) of **clm 1** and nucleic acids of **clm 12**.

The reference teaches “deprotecting” (or removal) of the protecting group (e.g. Claim 23; col. 2, lines 40+; Figure 9), which reads on step (b) of **clm 1**.

The reference teaches “determining the amount of unprotected active sites” (col. 2, lines 49+) by detecting the amount of cleaved “detectable label” (col. 2, lines 55+), which reads on step (c) of **clm 1**.

The reference teaches the detectable label (or protecting label) is a fluorescent label such as a rhodamine (e.g. Claims 26 and 27 of the reference), which reads on the “fluorescent groups” of **clm 2** and rhodamine of **clm 3**.

The reference teaches the fluorescent label is linked (or coupled) to the nucleotide (e.g. Figure 6), which reads on the “coupled to nucleobases” of **clm 13**. The instant specification and/or claims do not specifically define the phrase “coupled to nucleobase”. The phrase can be broadly interpreted to mean coupling the “protection group” (e.g. fluorescent label) and the “nucleobase” through any type of linkage (including both direct and indirect linkage). The reference teaches linking the fluorescent label through the phosphate group in the sugar group of the nucleotide (e.g. Figure 6), and thus the label is “coupled” to the nucleobase of the nucleotide.

Wagner et al

12. Claims 1-3 and 12-22 are rejected under **35 U.S.C. 102(b)** as being anticipated by Wagner et al (Helvetic Chimica Acta. Vol. 80: 200-212. 1997; cited in IDS filed on 9/22/04).

Wagner et al, throughout the publication, teach methods of nucleic acid synthesis using protected nucleotides. (see Abstract). The reference teaches synthesis of various oligonucleotides using protected nucleotides (pp. 204-206; especially Table 1 and p. 204, last para), which reads on step (a) of **clm 1**, and nucleic acids of **clm 12**.

The reference teaches “deprotection” of the nucleotides through removal of the protecting groups (e.g. p. 205, para 1-2; p. 204, para 3;), which reads on step (b) of **clm 1**.

The reference teaches “kinetic studies” of the deprotection process (e.g. p. 205, para 2), which reads on step (c) of **clm 1**.

The reference teaches the detectable label (or protecting label) is a fluorescent label such as a “dnseoc” (or a “dansyl”) (e.g. p. 201, para 3 and Figures), which reads on the “fluorescent groups” of **clm 2** and “dansyl” of **clm 3**. The “dnseoc” ((dansylethoxy)carbonyl) group also reads on the “L” group when n=1 (as recited in **clm 21**), because the carbonyl group reads on the formula “C(O)” and the dansyl group reads on formula “R”.

The reference teaches the fluorescent label is linked directly to the nucleobase (e.g. p. 202, Schemes 1-2), which reads on the “coupled to nucleobases” of **clm 13**, and coupling through the amino groups of **clm 14**.

The reference also teaches the structure of nucleotides comprising a base (protected by dnseoc), a sugar, a protected hydroxyl group, and a protected phosphate group (e.g. Scheme 2, Scheme 5). The (MeO)₂TrO (or Dimethoxytrityl) group in Scheme 5 of the reference (see p. 201, para 4 and p. 204) reads on the hydroxyl protection group, DMTrO (the elected species of ; see Reply, filed 3/6/07, p. 2) or the “triphenylmethyl” group of **clms 15, 16, and 17**.

The reference also teaches phosphate protection group such as the “(2-cyanoethoxy)bis(diisopropylamino)phosphine” at the 3’ sugar position (p. 204, para 1 and Scheme 5), which is the same phosphoramidite (phosphate amide) (i.e. the R3, R4, R5 and R6 groups of compound (f) in Figure 5 (the instant elected species; Reply, filed 3/6/07)), as recited in **clms 18, 19, and 20**. (Note: The instant Claim 19 is presumed to be providing additional

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structural limitations for the formulas recited in the instant claim 15. See the Rejection under 35 USC 112, 2nd paragraph).

The reference also teaches various nucleobases such as C, A, and G (e.g. p. 204, Scheme 5), which read on the nucleotide bases recited in **clm 22** and the elected species of adenine.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

14. Claims 1-3 and 12-22 are rejected under **35 U.S.C. 103(a)** as being unpatentable over Wagner et al (Helvetic Chimica Acta. Vol. 80: 200-212. 1997; cited in IDS filed on 9/22/04), in view of Hobbs et al (5,151,507; 9/29/1992) and if necessary, Chen et al (Journal of Organic Chemistry. Vol. 66: 1725-1732; 2001).

Wagner et al, throughout the publication, teach methods of nucleic acid synthesis using protected nucleotides, as discussed above in the rejection under 35 USC §102.

Wagner et al do not specifically teach using “stilbene” (the elected species) as the “fluorescent group”, as recited in **clm 3**.

However, Hobbs et al teach using various fluorescent molecules to label (or protect) nucleotides (see Abstract). The reference teaches “stilbene” can be used to attach to the

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nucleobases (col. 30, lines 20+) through linkers that comprise “carbonyl” group (reads on the formula of “COR” of **clm 21**; col. 11, lines 50+). The reference also teaches various fluorescent dye can be used depending on the different applications (cols. 12+).

In addition, Chen et al, teaches attaching “stilbene” to nucleosides (see Abstract). The Chen reference also teaches “stilbene” has “bright fluorescence of very high quantum yield” (p. 1725, right col., para 2).

Therefore, it would have been prima facie obvious for one of ordinary skill in the art at the time the invention was made to attach a fluorescent group such as “stilbene” to a “monomeric building block” (such as a nucleoside).

A person of ordinary skill in the art would have been motivated at the time of the invention to use “stilbene” as the “detectable protecting group”, because “stilbene” is a known fluorescent label for biomolecules (especially nucleotides), and stilbene is known to exhibit “bright blue fluorescence of very high quantum yield”, as taught by both Hobbs et al and Chen et al.

A person of ordinary skill in the art would have reasonable expectation of success of achieving such modifications since both Hobbs et al and Chen et al have demonstrated successful attachment of various fluorescent groups (especially stilbene) to nucleosides through known reaction mechanisms (such as the formation of -HN-C=O linkage between the nucleobases and the stilbene molecule), as demonstrated by the said references.

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Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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Art Unit 1639
4/2/2007


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SUPERVISORY PATENT EXAMINER